REMARKS

Claims 1-4, 6-10, 18-24 and 35 were in the case prior to this amendment. Claim 35 has been amended above. Claims 1-4, 6-10, 18-24 and 35 remain in the case.

Rejections under 35 USC § 112, second paragraph

The Examiner rejected claim 35 as being indefinite stating that "majority" is a relative term which would cause one of ordinary skill in the art not to be reasonably appraised of the scope of the invention. Applicants respectfully traverse this rejection. The specification makes it clear that the inventive composition comprises colloidal silver particles having certain defined physical characteristics. It is demonstrated in the specification that these silver particles are unusually efficacious as compared to other silver products. As is explained in the specification, as well as in the prior art cited by the Examiner, there is an extremely long history showing that silver ions and at least some compositions containing metallic silver show antimicrobial—particularly antibacterial—properties. As is also well known in the art, excessive treatment with silver ions can result in skin discoloration (agyria) as well as other more serious problems. Therefore, there has been a search to find silver products which are effective at minimal silver concentrations and contain no detectable silver ions. Applicants' composition is a mixture of colloidal silver particles having a certain range of sizes. Applicants chose to describe their mixture by characterizing the total amount of silver and the range of particles sizes because the sizes of the particles describes the surface to volume characteristics of the material. It will be appreciated by those of ordinary skill in the art that it can be difficult to produce exact size distributions of nano-scale particles. Further, it will be appreciated that the precise size distribution necessarily varies somewhat from batch to batch of the material.

In the specification (see particularly pages 5-7) the size distribution of a preferred composition is characterized by stating that the composition contains particles where more than 50% of the particles (a majority of the particles) have a maximum dimension

of less that 0.015 micrometers (15 nm). Furthermore, a majority of the particles have a minimum dimension of more than 0.002 micrometers (2 nm). In a preferred embodiment more than 75% of the particles have a minimum dimension greater than 0.005 micrometers (5 nm). Other information is also given—for example more than 90% of the particles have a maximum dimension of less than 0.02 micrometers (20 nm). From these descriptions one of skill in the art would understand that majority (more than half) of the particles would fall in the range 5 nm—15 nm. The dimensions are provided to enable one to determine whether a particular silver composition falls within the scope of the invention. One of ordinary skill in the art would clearly understand that "majority" of the particles means more than 50%. If more than half of the particles in a colloidal silver suspension meeting the other criteria of the claim 1 falls within the bounds of claim 35, then that claim is met. Applicants respectfully contend that this is the well understood meaning of the word "majority" and that such language is often used is often used to describe the size distribution of particles.

Claim rejections under 35 USC § 103

The Examiner rejected claims 1-4, 8-10, 18-24 and 35 as being unpatentable over US Published Patent Application No. 20030054046 (now U.S. Paten No. 6,939,568). Applicants respectfully traverse this finding as will be detailed below. However, Applicants do appreciate the careful manner in which the Examiner has laid out the Graham factors. Nevertheless, Applicants respectfully suggest that the Graham factors as considered by the Examiner are not precisely those spelled out by the Supreme Court. The Examiner's attention is drawn to 148 USPQ 467, paragraph 8 where the Court clearly states: "Under § 103, the scope and content of the prior art are to be determined; differences between the prior art and the claims at issue are to be ascertained; and the level of ordinary skill in the pertinent art resolved. Against this background, the obviousness or nonobviousness of the subject matter is determined." The Court goes on to discuss the importance of secondary consideration which will not be discussed in the present case at this time. Section 2141 of the MPEP summarizes

these factors as: (A) Ascertaining the differences between the claimed invention and the prior art; and (B) Ascertaining the differences between the claimed invention and the prior art; and (C) Resolving the level of ordinary skill in the pertinent art. Clearly, there is some sort of typographical error in the MPEP since (A) and (B) are identical. Applicants believe that (A) was intended to read something like "Determining the scope and content of the prior art." Undoubtedly, this obvious mistake has already been pointed out to the authors of the MPEP. Applicants are not certain from where the summary of the Graham factors presented on Page 3 of the Office Action were derived, but they do appear to conflate the normally accepted Graham factors.

This change in factors has affected the prima facie case laid out by the Examiner. The traditional Supreme Court analysis suggests first determining the scope and content of the prior art, and then ascertaining the difference between the claimed invention and the prior art. The level of ordinary skill in the art is then determined and this background is used to make a determination of obviousness or nonobviousness. To guide this determination the MPEP follows the guidance of KSR to provide "rationales" of obviousness (MPEP §2142-2143). The important point is that no matter what rationale is followed one of ordinary skill in the art must have had a reasonable expectation of success in making the combination. That is, there must have been reasonable predictability. Clearly, if the level of ordinary skill in the art is not clearly determined, it will not be possible to demonstrate that one of ordinary skill would have had a reasonable expectation of success or that the outcome was reasonably predictable.

Applicants respectfully contend that the Examiner has not succeeded in making out a prima facie case of obviousness. In ascertaining the scope and content of the prior art, the Examiner concentrated only on the one piece of art being used in the combination. Also, the level of ordinary skill in the art was not explicitly or implicitly determined. This made it impossible to determine whether differences between the claimed invention and the prior art were such that one of ordinary skill in the art would have a reasonable expectation of success—namely that there was reasonable

predictability. This also makes it impossible to make a valid determination that one of ordinary skill would have had a reasonable expectation of success. Applicants believe the failure to determine the level of ordinary skill in the art can also be seen in the earlier discussed rejection under 35 USC § 112, second paragraph. In that rejection the Examiner argued that one of ordinary skill in the art would not have understood the scope of the invention from the claim language. Without usurping the Examiner's job of determining the level of ordinary skill in the art, Applicants respectfully point out that both the instant specification and Burrell et al. deal with the dimensions of very small particles. Applicants respectfully contend that part of the skill set held by one of ordinary skill in this art area would include an understanding of the way of expressing measurements of populations of particles, including an understanding that "majority of particles" means that at least half the particles in the population have a certain specified characteristic.

Not only did the Examiner not determine the level of ordinary skill in the art and the scope of the prior art as a whole, in characterizing Applicants' claimed invention the Examiner did not give reasonable interpretation to the clearly expressed claim elements. Applicants' composition comprises an antibacterial hydrogel composition consisting of a hydrophilic polymer (the gelling component) and colloidal silver particles (the antibacterial component) providing between 5 and 40 ppm silver wherein the silver particles have an elemental silver interior and a silver oxide exterior. A fair reading of the instant specification shows that the basic invention is that colloidal silver particles having the claimed characteristics show unusually strong antimicrobial properties. This is demonstrated in test after test where very low overall concentrations of silver show tremendous effectiveness. As admitted in the instant specification, antimicrobial properties of silver—particularly silver ions—are well known. The instant invention is a composition showing exceptional effectiveness at low overall concentrations of silver. Further, it was discovered and demonstrated that the colloidal silver particles retained their effectiveness when combined with a gelling agent to form a hydrogel. A proper determination of the scope of the prior art would show a large number of hydrogels

based on ionic silver—such as silver sulfadiazine. However, since silver particles probably do not diffuse through gels as readily as silver ions, it was not expected that the particles would be effective in a gel base.

In comparing the claimed invention to Burrell et al. the Examiner demonstrated Burrell et al. teaches the use of "nanocrystalline" silver coating. In Example 11 No. 2 the silver was coated directly onto carboxymethyl cellulose (CMC) fibers which were directly used to produce a hydrogel. The hydrogel generated a 5.2 log reduction of *Pseudomonas aeruginosa*. The Examiner further pointed out that the "nanocrystalline" silver coating was produced with a base layer of silver metal with a silver oxide top coating. Although the silver level in the CMC gel was not disclosed, the Examiner pointed out that Burrell et al. teaches that the silver level in the various inventive preparation ranges from 1 ppm to 5,000 ppm. Note that Burrell et al. does not teach the use of colloidal silver particles with a silver oxide coating showing effectiveness as 5 to 40 ppm total silver.

In ascertaining the difference between Burrell et al. and the claimed invention, the Examiner concludes that Burrell et al. does not exemplify a hydrogel with a concentration of from 5 to 40 ppm. However, the Examiner concludes that because Burrell discloses concentration of 1 ppm to 5000 ppm one would have been motivated to use an amount of silver in this range. Applicants traverse this finding of obviousness because, among other things, the Examiner has failed to give a reasonable interpretation of the claimed invention in making this rejection. The primary claim of the Applicants' invention calls for an antimicrobially effective hydrogel containing from 5 ppm to 40 ppm silver in the form of colloidal silver particles having a silver interior and a silver oxide exterior. Burrell et al. do not teach colloidal particles having this composition. Burrell et all teaches a nanocrystalline silver coating that may have a top layer of silver oxide. Thus, even if the coating were broken up to form colloidal particles, such particles would have silver oxide on only one side.

Although Burrell et all does teach silver compositions having a total silver concentrations between 1 and 5,000 ppm (a tremendous range), there is little, if any

demonstration of efficacy within the silver concentration range demonstrated to be efficacious with Applicants' invention. Many of Burrell et al. compositions have extremely high levels of silver (example No. 4 (paragraph 0239) contains 1000 ppm silver). In many cases it is difficult to determine what concentration of silver was actually in solution. Paragraph 0195 does demonstrate that the level of silver in solution was 66 ppm so it seems reasonable to assume that silver materials prepared according to Burrell et al. contain this amount of silver in solution. Note that in Applicants' invention all the silver is in solution at levels between 5 ppm and 40 ppm.

There is no evidence that the Burrell et al. hydrogel (the CMC) hydrogel cited by the Examiner is effective at a level of between 5 and 40 ppm silver. Applicants have explained the advantage of the unexpectedly low silver level at which their invention is effective. There is no evidence that the CMC gel contains colloidal silver particles. The silver coating is disclosed to contain microcrystalline grains which are believed to result in release of "silver clusters" but the silver clusters (14 atom by 14 atom cubes) are not colloidal particles as claimed in the present invention since it is know that silver particles having a diameter of 5 nm contain around 3900 atoms. Therefore, the "silver clusters" must be much smaller than Applicants' colloidal particles. As pointed out above even if the nanocrystalline coating was broken up to form colloidal particles, those particles would not be coated by silver oxide as required in the claims.

The Examiner reduces the differences between the claimed invention and the prior art to only the level of silver in the hydrogel and then concludes that it would be obvious to vary that concentration. The Examiner contends the ranges of Applicants' invention and that Burrell et al overlap. Applicants respectfully contend that this entirely misses the point. First, as pointed out above, the demonstrated effective ranges of Applicants' invention do not overlap with the demonstrated effective ranges of Burrell et al. Burrell et al. do not teach an effective antimicrobial hydrogel containing only 5 ppm to 40 ppm total silver. Second, Applicants teach colloidal silver particles with a silver oxide coating wherein the particles are highly effective at total silver concentration of 5 ppm to 40 ppm. Burrell et al. teach a nanocrystalline coating. Even if that coating is broken up

to yield particles, those particles do not have the silver oxide coating claimed by Applicants. Applicants teach the importance of silver colloidal particles of a particular composition.

Thus, one of ordinary skill in the art realizing the tremendous range of silver compositions possible is expected to look at Burrell et al. and deduce that switching from nanocrystalline coatings to colloidal silver particles wherein the particles are coated with silver oxide would result in unexpectedly improved efficacy at lower silver concentrations. Applicants respectfully contend that the Examiner has failed to provide evidence that one of ordinary skill in the art would perceive a reasonable expectation of success in the absence of the teachings of Applicants' disclosure. Therefore, the prima facie case of obviousness must fail.

The Examiner further rejected claims 6-7 as being unpatentable over Burrell et al. in view of Schonfeld et al. The Examiner states that Burrell et al. does not teach the use of hydrogen peroxide in a silver containing hydrogel. However, Schonfeld et al. which is directed to color stabilization of a silver containing hydrogel, overcomes this lack. The Examiner concludes that one of ordinary skill in the art would be motivated to utilize hydrogen peroxide in order to produce color stabilization as taught by Schonfeld et al. Applicants respectfully traverse this prima facie case of obviousness. Applicants teach that adding hydrogen peroxide can produce synergistic antimicrobial results with their particular silver composition. Without tests it is not possible to determine whether this effect would occur with other silver compositions. Schonfeld et al. was not concerned with synergistic antimicrobial effects. Rather, Schonfeld et al. was concerned with controlling a cosmetic defect (uneven color formation) that occurs when a silver ion product is polymerized into a gel using electron beam radiation. There is no teaching that hydrogen peroxide contributes to the efficacy of the gel. Nor is there any teaching that hydrogen peroxide is effective to reduce color in the absence of magnesium trisilicate (see examples XI-XII in column 5). Applicants' gel <u>does not contain</u> magnesium trisilicate; Neither Applicants' gel nor that of Burrell et al. shows any discoloration—perhaps because these gels do not contain ionic silver or perhaps

because electron beam radiation is not used to polymerize the gels. In any case Schonfeld et al. is not directed to solving the same problem (antimicrobial efficacy) dealt with by Applicants. All of these facts would suggest that this prior art is not reasonably combinable with Burrell et al. In any case there is nothing in Burrell et al. or in Schonfeld et al. and any combination of these references that would suggest to one of ordinary skill in the art that adding hydrogen peroxide to Applicants' gel would result in improved antimicrobial properties. The prima facie case of obviousness must fail.

In view of the foregoing, it is respectfully submitted that the application is in condition for allowance. Reexamination and reconsideration of the application, as amended, are requested. If for any reason the Examiner still finds the application other than in condition for allowance, the Examiner is requested to call the undersigned attorney at the Los Angeles telephone number (310) 229-9928 to discuss the steps necessary for placing the application in condition for allowance.

You are hereby authorized to charge any fees due and refund any surplus fees to our Deposit Account No. 22-0261. Please reference matter number 80663.251821.

Respectfully submitted,

VENABLE LLP

Date: 9-Oct-2008

By: /Stefan J. Kirchanski/
Stefan J. Kirchanski
Registration No. 36,568
Attorney for Applicant(s)

2049 Century Park East, 21st Floor
Los Angeles, CA 90067
Telephone: (310) 229-9900
Facsimile: (310) 229-9901
Email: SJKirchanski@venable.com